REMARKS

Reconsideration is requested.

Claims 20-38 are pending. The above amendments find support throughout the specification. No new matter has been added.

The Office Action of December 23, 2004 indicates on page 1 that the Office Action is both a final and a non-final Office Action. The applicants presume that the Office Action is a non-final Office Action as the concluding paragraphs of the Office Action do not contain an indication that the Office Action is a final Action and page 2 of the Office Action indicates that the new grounds of rejection were not necessitated by the applicants previous amendments. The Examiner is requested to advise the undersigned in the event the Office Action of December 23, 2004 is a final Action.

The objections of claims 22 and 35 noted on page 2 of the Office Action dated December 23, 2004, are obviated by the above amendments.

To the extent not obviated by the above amendments, the Section 112, second paragraph, rejection of Claims 23-24, 26, 28-29 and 34 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following further comments.

The objected-to phrase "moderate promoter" has been deleted, without prejudice. The term "moderate" will be recognized by one of ordinary skill in the art and the amendments have been made solely in order to promote the progress of this application.

Claim 26 has been revised to confirm that the "enzymes" synthesize the neurotransmitter.

Claim 28 has been amended to include the article "a".

The Examiner alleges that with regard to claim 28 that the term "minimal CMV promoter" is not particularly defined in the specification and that it is not clear if "minimal CMV promoter" means a CMV promoter lacking enhancer elements and if the minimal CMV promoter contains the prescribed "tetOP" sequences.

The applicants believe that one of ordinary skill in the art will appreciate that the phrase "minimal CMV promoter" refers to a CMV promoter lacking enhancer elements and that the "tetOP" sequences have been added to this minimal promoter. The specification at page 10, lines 20-25 states the following:

> "*such a promoter comprises the minimum elements which are essential for transcriptional promoter function (for exemple the TATA box) and lacks the other regions which are naturally involved, for example, in the strength of the promoter or in its regulation*"

and page 12 lines 1-4 describes the following:

> "*the original promoters can be digested with enzymes and tested for their activity, preferably after they have been functionally coupled to one or more Op sequences.*".

Claim 28 is believed to clearly state that the minimal CMV promoter is functionally coupled to the "tetOP" sequences. Furthermore, the applicants submit that one of ordinary skill in the art is well aware of the metes and bounds of a minimal CMV promoter.

The claims are submitted to be definite and withdrawal of the Section 112, second paragraph, rejection is requested.

The Section 102 rejection of claims 20-27, 29 and 31-32 over Bujard (U.S. Patent No. 5,650,298), is traversed. Reconsideration and withdrawal of the Section 102 rejection are requested in view of the following distinguishing remarks.

FIG 13 of the cited patent is understood to show the targeting construct integrated into the genome. The nucleic acid of the present claims, such as claim 20, however, is an isolated product. The subject matter of claim 20, for example, therefore is submitted to be clearly different from the nucleic acid of FIG 13 which is integrated into the genome. Moreover, claim 20 specifies that the first promoter and the nucleic acid of interest are not from the same gene.

The cited patent, in FIG13, is understood to describe, at best, a nucleic acid wherein the nucleic acid encoding tTA, the transcriptional terminator and the tetracycline sensitive promoter are flanked on one side by sequences of the regulating sequence of the endogenous gene and on the other side by sequences of the coding sequence of the same endogenous gene.

The claims are submitted to be patentable over Bujard et al ('298) and withdrawal of the Section 102 rejection over the same is requested.

The Section 103 rejection[1] of claims 20-27, 29, 31-33 and 36 over Bujard in view of Courti (NeuroReport, 1996; 7:1655-1659), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing remarks.

[1] The Examiner's statement of the rejection on page 7 of the Office Action dated December 23, 2004, specifically states that the rejection is made pursuant to 35 U.S.C. 102(b) however the whole of the Examiner's arguments and preceding paragraphs spanning pages 6-7 of the Office Action suggest that the rejection is actually made pursuant to 35 U.S.C. 103. The applicants have therefore presumed the rejection has been made pursuant to 35 U.S.C. 103 and the Examiner is requested to advise the undersigned in the event this is an incorrect presumption, and to mail a new Office Action with the date

As detailed above, the '298 patent fails to disclose an isolated nucleic acid according to the claimed invention. The Examiner's secondary reference is not believed to cure the deficiencies of the primary reference.

Specifically, the cited art is not believed to have made it obvious to provide an isolated nucleic acid which contains (a) a first region which contains a nucleic acid which encodes the transactivator of the tetracycline-regulated system (tTA) under the control of a first promoter which is a non-viral promoter, and (b) a second region which contains a nucleic acid of interest under the control of a second promoter which is a tTA-sensitive promoter, and wherein the two regions (a) and (b) are arranged in the same transcriptional orientation and the first promoter and the nucleic acid of interest are not from the same gene.

Therefore, the '298 patent fails to disclose that the first promoter and the nucleic acid of interest are not from the same gene. Further, the patent could not have taught or suggested that the first promoter and the nucleic acid of interest could be from different genes for the following reasons. As the tTA system disclosed in the '298 patent is aiming to be used in homologous recombination, the flanking sequences have to be from the same endogenous gene. Consequently, the first promoter and the coding sequence under a tetracycine sensitive promoter are from the same endogenous gene.

Corti et al teaches a construct that comprises a tTa system under control of a CMV promoter (viral promoter) as well as a reporter gene under a minimal CMV promoter with the two transcription units being separated by a UMS sequence. This

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reset for responding which details the elements of Section 102 in the event the Examiner actually meant to assert that the noted claims were anticipated by the cited combination of art.

construct is incompatible with homologous recombination. Therefore, the person of ordinary skill in the art would not have combined the '298 patent with Corti et al., as suggested by the Examiner.

Moreover, Corti et al do not disclose or suggest a tTA system under the control of a non-viral promoter. Furthermore, the person of ordinary skill in the art would not have combined Corti et al with the '298 patent because the goal of the '298 patent is understood to only be to insert a tTA system into an endogenous gene and not to provide a nucleic acid of the presently claimed invention.

Claims 20-27, 29, 31-33 and 36 are submitted to be patentable over Bujard in view of Corti and withdrawal of the Section 103 rejection of these claims over the same is requested.

The Section 103 rejection of claims 20-27, 29, 30, 31, 32, 33 and 36-37 over Bujard, Courti and Hu (Cancer Research 1997; 57:3339-3343), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following further comments.

The deficiencies of Bujard and Corti are noted above. The cited Hu reference is not believed to cure these deficiencies.

Specifically, Hu et al are understood to teach a construct that comprises a tTa system under control of a minimal CMV promoter (a viral promoter). Hu et al. do not disclose or suggest a tTA system under the control of a non-viral promoter. This construct is incompatible with homologous recombination. Therefore, the person of ordinary skill in the art would not have combined the '298 patent with Hu et al.

The person of ordinary skill in the art would not have combined Hu et al with the '298 patent because the goal of the '298 patent is to only insert a tTA system into an endogenous gene and not to provide a nucleic acid of the presently claimed invention. Moreover, the authors of the cited art provide no motivation to change the minimal CMV promoter by a non-viral promoter.

The claims are submitted to be patentable over Bujard, Courti and Hu. Withdrawal of the Section 103 rejection based on the same is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required.

The Examiner is requested to confirm that the drawings filed May 8, 2001 are acceptable.

Respectfully submitted,

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